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### Coping styles and aggression

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## Chapter 2

# Coping Styles and Aggression: A Biobehavioral Approach

Jaap M. Koolhaas and Sietse F. de Boer

### Introduction

Health and stress-related disease are generally considered to be influenced by a complex interplay between the actual environmental demands and the individual's capacity to cope with these demands. A wide variety of medical, psychological, and biological studies both in humans and in animals demonstrate that individuals may differ in their capacities to cope with such environmental demands. Factors that have been shown to affect the individual coping capacity include genotype, ontogeny, adult experience, age, social support, and so forth. For ages, researchers have tried to determine the individual vulnerability to stress-related diseases using estimates of the individual coping capacity. These attempts date back to the times of Hippocrates who distinguished the following four temperaments: choleric, sanguine, phlegmatic and melancholic. Each of these temperaments was supposed to reflect a general attitude in dealing with everyday problems. More recent approaches use the concept of coping and try to classify coping responses into distinct coping strategies. Psychologists define coping in humans as the cognitive, behavioral, and emotional ways of managing stressful situations. According to Lazarus (1966), coping responses are determined by the appraisal of the degree of control over important resources available to the individual. In their conceptualization, psychologists divide coping responses into emotion-focused coping and problem-focused coping strategies. The concept of coping is also used by biologists to understand the behavioral and physiologic ways animals manage stressful conditions. A coping strategy can therefore be defined as a coherent set of behavioral and physiologic stress responses that is consistent over time and context and that is characteristic of a certain group of individuals. Most studies describe individual differences in behavior and physiology as trait characteristics that may determine the individual's vulnerability to stress-related diseases.

These studies are in the realm of biomedical sciences, yet there is a growing interest in individual differentiation in behavior and physiology in the science of ecology and evolutionary biology (Sih, Bell, Johnson, & Ziemba, 2004). Individual variation in coping with challenges in the natural habitat is not only considered as the origin of speciation but may be an important factor in the regulation of populations as well. It seems that coping strategies have been shaped by evolution and

form general adaptive response patterns in reaction to everyday challenges in the natural habitat. The aim of this chapter is to describe coping strategies in animals as they might be observed in nature and to summarize the available evidence of their possible function. We will focus on aggressive behavior as an important indicator and component of coping strategy. It will be argued that the individual variation in aggressive behavior is related to a differentiation in behavioral flexibility. This differential degree of flexibility seems to be one of the major factors involved in the differential fitness of individuals under various environmental conditions in nature.

## Aggression and Coping Strategies

Much of our current thinking on coping strategies is based on the work of Jim Henry (Henry & Stephens, 1977). He suggested, on the basis of social stress research in animals and man, that two different stress response patterns may be distinguished. The first type, the active response, was originally described by Cannon (1915) as the fight-flight response. Behaviorally, territorial control and aggression characterize this active response. Engel and Schmale (1972) originally described the second type of stress response as the conservation-withdrawal response. This response pattern is characterized behaviorally by immobility and low levels of aggression. These authors consider the degree in which animals react with an aggressive response to a stressor as an important discriminating factor of the two coping strategies. These ideas led to the expectation that the individual level of aggressive behavior (i.e., the tendency to defend the home territory) is related to the way individual male mice react to environmental challenges in general. This hypothesis was tested by Benus, Bohus, Koolhaas, and Van Oortmerssen (1991a) using male house mice that were genetically selected for either short attack latency (SAL) or a long attack latency (LAL). These selection lines of wild house mice were derived from a completely different line of research aimed at investigating the genetic basis of aggression. Also, when other indices of aggressive behavior are taken into account, the SAL males are considered extremely aggressive, whereas the LAL males have very low levels of intermale aggressive behavior. The results of a series of experiments in mice and rats, which are summarized in Table 2.1, demonstrate that the individual tendency to initiate aggressive behavior is indeed predictive of the individual reactions to other, nonsocial environmental challenges. This pattern of behavioral responses is consistent with the concept of stable coping strategies.

Table 2.1 shows that the individual level of aggressive behavior is related to the way in which the animals react to a wide variety of environmental challenges. It seems that aggressive males have a strong tendency to take the initiative (i.e., attack, active avoidance, or nest building). Nonaggressive males seem to accept the situation more easily as it is, responding only when absolutely necessary. This difference in response initiation forms the basis of the terminology we currently use for the different coping strategies. In our view, high levels of aggression are a reflection of

**Table 2.1** Summary of the behavioral differences between high-aggressive and low-aggressive male rats and mice

Behavioral characteristics	High aggressive	Low aggressive
<b>Tests for proactivity</b>		
Attack latency	Low	High
Active avoidance	High	Low
Defensive burying	High	Low
Nest building	High	Low
<b>Behavioral flexibility tests</b>		
Routine formation	High	Low
Cue dependency	Low	High

Source: Koolhaas, J. M., Korte, S. M., De Boer, S. F., Van Der Vegt, B. J., Van Reenen, C. G., Hopster, H., et al. (1999). Coping styles in animals: current status in behavior and stress-physiology. *Neuroscience & Biobehavioral Reviews*, 23, 925–935.

a more general proactive coping strategy, whereas a low level of aggression reflects a reactive coping strategy.

An important fundamental question is whether the two types of behavior patterns can be considered to represent strategies of coping in the sense that they are both aimed at successful environmental control. Several experiments indicate that the different behavior patterns can indeed be considered as coping strategies. An illustrative example is the shock prod defensive burying test. In this test, the animal is confronted with a small, electrified prod in its home cage. Because this prod is a novel object, the experimental animal will explore it by sniffing at the object. Consequently, the animal receives a mild but aversive shock. As soon as it has experienced the shock, the animal has two options to avoid further shocks. It may either hide in a corner of the cage to avoid further contact with the shock prod or it may actively bury the shock prod with the bedding material of the cage. Under these free-choice conditions, aggressive males spend most of the 10 minutes of test-time burying, whereas nonaggressive males show immobility behavior. Notice, however, that the two types of responding are equally successful in avoiding further shocks (De Boer & Koolhaas, 2003). In this particular test, successful coping can be defined operationally as avoidance of further shocks. In that sense, both response types in the defensive burying test can be considered as successful coping. However, Treit, Pinel, and Fibiger, (1981) described the defensive burying test originally as an anxiety test. High levels of burying behavior would indicate a high level of anxiety. Therefore, one may argue that the differences in burying behavior reflect a difference in baseline emotional state such as anxiety. We think that this interpretation is not correct. When high and low aggressive males (rats and mice) are tested in a well-validated anxiety test, the elevated plus maze, no differences are observed. The difference between both anxiety tests is that the elevated plus maze is more a test for baseline anxiety, whereas the burying test is a test for fear induced by the electric shock. In line with the concept of proactive and reactive coping, this fear can be expressed either as burying behavior or as immobility behavior (De Boer, Van Der Vegt, & Koolhaas, 2003).

It is important to emphasize that the differentiation in coping strategies may not be expressed equally clearly in all challenging situations. In particular, tests that measure aspects of initiative or proactivity seem to be most discriminative. This holds, for example, for latency measures such as the attack latency test in males or the defensive burying test, which allow the animal a choice between proactive and reactive coping. Although female mice usually do not show territorial aggression, females of the short attack latency selection line show much more defensive burying than female mice of the long attack latency selection line. This supports our view that aggression is only one of a larger set of behavioral characteristics that make up the proactive coping strategy.

## **Behavioral Flexibility**

The concept of coping strategies is basically descriptive; that is, it describes the correlations and consistencies of the behavior of individual animals under different environmental conditions. The question is to what extent these differences might be causally related to differential cognitive abilities? Several experiments indicate that proactive and reactive coping strategies differ in the degree to which behavior is guided by environmental cues (Koolhaas et al., 1999). Aggressive males easily develop routines (i.e., a rather intrinsically driven rigid type of behavior). Nonaggressive males are more flexible and react to environmental stimuli all the time. This can be demonstrated for example by the way in which aggressive and nonaggressive males react to a small change in an otherwise stable environment. Animals can be trained to run a maze for a food reward. Rats and mice can learn such a task easily. When they reached a stable task performance, the reaction to a small change in the maze was studied. In one experiment, a small piece of tape was put on the floor in one of the alleys of the maze, while in another experiment, the maze was turned 90 degrees with respect to the extra maze cues. In both experiments, aggressive males paid little or no attention to the change (i.e., there was no increase in time to complete the task and no increase in the number of errors made in the maze). Nonaggressive males, on the other hand, started exploring the maze again and hence took much more time to get to the goal box and made more errors in the task. This suggests that the behavior of the nonaggressive male may be much more guided by environmental stimuli, whereas aggressive males seem to develop routines. A similar difference in behavioral plasticity can be demonstrated in the response to a 12-hour shift in light-dark cycle. Aggressive male mice stay in their original day-night rhythm for a few days after which their rhythm gradually shifts to the new cycle. Nonaggressive males on the other hand shift their rhythm immediately; they are twice as fast in adapting to the new light-dark cycle as the aggressive males (Benus, Koolhaas, & Van Oortmerssen, 1988).

These experiments show that the two coping strategies differ more generally in the use of feedback and feed-forward behavioral control. The proactive animal acts primarily on the basis of previous experience (i.e., feed-forward control). The

reactive coping animal seems to rely on feedback information. This fundamental difference in behavioral control may causally explain why the animals differ in such a wide variety of behavioral tests. One may conclude that the concept of coping strategies can be reduced to an underlying difference in a limited number of behavioral control mechanisms. Moreover, this differential use of behavioral control mechanisms also relates to the adaptive character of the two coping strategies. A proactive coping animal may be adapted to stable environmental conditions. After all, a feed-forward behavioral control works best under highly predictable conditions. The reactive coping strategy may do better under variable and unpredictable environmental conditions. Indeed, field studies on feral mouse populations indicate that aggressive males are more successful under stable colony conditions, whereas nonaggressive males do better during migration (see below).

## Neuroendocrinology of Coping Strategies

Coping strategies are not only characterized by differences in behavior but also by differences in physiology and neuroendocrinology. As mentioned earlier, tests that measure aspects of initiative or proactivity seem to be most discriminative. The defensive burying test in rodents is such a test, which allows the animal a choice between proactive and reactive coping. In general, high plasma noradrenalin and relatively low plasma adrenaline and corticosterone accompany defensive burying, whereas freezing behavior is associated with relatively low plasma noradrenalin and high plasma corticosterone levels. In a strain of wild-type rats, the more aggressive males showed the highest levels of burying behavior and showed a larger catecholaminergic (both plasma noradrenalin and adrenaline) reactivity after electrified prod exposure than did the nonaggressive rats (Sgoifo, De Boer, Haller, & Koolhaas, 1996). Also, during social defeat, the more competitive proactive male rats react with higher responses of blood pressure and catecholamines than the more reactive rats. In addition, these competitive males had higher baseline levels of noradrenalin (Fokkema, Smit, Van der Gugten, & Koolhaas, 1988). The same can be observed in a comparison between strains. The aggressive wild-type rats responded to social defeat with larger sympathetic (plasma noradrenalin levels) reactivity and concomitantly lower parasympathetic reactivity (as measured by increased heart rate response and decreased heart rate variability) than the less aggressive Wistar rats (Sgoifo et al., 1997). Thus, proactive coping rodents show in response to stressful stimulation a low Hypothalamus-Pituitary-Adrenocortical (HPA) axis reactivity (low plasma corticosterone response) but high sympathetic reactivity (high levels of catecholamines). In contrast, reactive coping rodents show higher HPA-axis reactivity and higher parasympathetic reactivity (Table 2.2). Differences in endocrine activity have also been observed for HPA axis and gonadal axis activity under baseline conditions. In aggressive mice, reduced circadian peak plasma corticosterone levels have been observed compared with nonaggressive mice (Korte et al., 1996). In mice of the short attack latency selection line and in wild-type male rats, high baseline levels of testosterone have been observed, while the proactive coping male

**Table 2.2** Summary of the physiologic and neuroendocrine differences between proactive and reactive animals

Physiologic and neuroendocrine characteristics	Proactive	Reactive
HPA-axis activity	Low	Normal
HPA-axis reactivity	Low	High
Neurosympathetic reactivity	High	Low
Adrenomedullary reactivity	High	Medium
Parasympathetic reactivity	Low	High
Testosterone production	High	Low
Testosterone sensitivity	High	Low

is also more sensitive to the behavioral effects of testosterone (Ruiter, Koolhaas, Keijser, Van Oortmerssen, & Bohus, 1992).

## Neurobiology of Coping Strategies

Several studies in our rats and mice show a widespread central nervous differentiation between the two coping strategies. This takes place, for example, at the level of the peptidergic modulation of the central nucleus of the amygdala (Roozendaal, Wiersma, Driscoll, Koolhaas, & Bohus, 1992), the vasopressinergic neurons in the bed nucleus of the stria terminalis and its innervation of the lateral septum (Compaan, Buijs, Pool, De Ruiter, & Koolhaas, 1992), the suprachiasmatic nucleus (Bult, Hiestand, Van der Zee, & Lynch, 1993), postsynaptic 5-HT<sub>1a</sub> receptor sensitivity, the hippocampal mossy fiber system (Sluyter, Jamot, Van Oortmerssen, & Crusio, 1994), and striatal dopaminergic mechanisms (Benus, Bohus, Koolhaas, & Van Oortmerssen, 1991b). These differences reflect differences in the state of brain mechanisms in terms of number of neurons, degree of arborization of neurons, hormonal and neurotransmitter receptor binding capacity, and so forth, which in concert may determine the tendency to cope either proactively or reactively with environmental challenges.

It is interesting to notice that the vasopressinergic system of the lateral septal area is well-known to be sexually dimorphic and testosterone dependent. Males are characterized by a considerably higher density of Lateral Septum Arginine Vasopressin (LS-AVP) fibers than females. However, the differences in density of LS-AVP fibers as observed in the proactive and reactive coping strategies within the male gender turn out to be as large as the differences between the sexes. This indicates that the differentiation in coping strategies is somehow related to the differentiation between the sexes. Indeed, there is some evidence that the perinatal processes involved in the sexual differentiation are also involved in the development of the two coping strategies within the male gender (Koolhaas, Everts, de Ruiter, De Boer, & Bohus, 1998).

An intriguing recent observation in mice indicates that the nonaggressive, reactive coping mouse shows the strongest hippocampal neuronal plasticity in terms of stress-induced changes in hippocampal neurogenesis. This is correlated with a

**Table 2.3** Summary of the central nervous differences between proactive and reactive male rats and mice

Neurochemical characteristics	Proactive	Reactive
Septum AVP-ir fibers	Low density	High density
SCN AVP-ir fibers	Low density	High density
AVP infusion in ACE	Insensitive	Immobility
AVP infusion in ACE	Insensitive	Bradycardia
CRH infusion in ACE	Behavioral activity	Insensitive
CRH infusion in ACE	Tachycardia	Insensitive
Hippocampal mossy fibers	Small	Large
Striatal dopamine	Sensitive	Insensitive
5-HT turnover	High	Low
5-HT1a binding	High	Low
5-HT1a receptor mRNA	High	Low
5-HT1a receptor sensitivity	High	Low

AVP-ir, Arginine Vasopressin Immunoreactivity; SCN, Suprachiasmatic Nucleus; ACE, Central Amygdala; CRH, Corticotropin Releasing Hormone; 5-HT, 5-hydroxytryptamine.

significantly higher hippocampal expression of genes coding for cytoskeleton proteins (Feldker, De Kloet, Kruk, & Datson, 2003).

## Stress Vulnerability

The concept of coping styles implies that animals have a differential capacity to adapt to various environmental conditions. Negative health consequences might arise if an animal cannot cope with the stressor or needs very demanding coping efforts. In view of the differential neuroendocrine reactivity and neurobiological makeup, one may expect different types of stress pathology to develop under conditions in which a particular coping style fails. Although there are only a limited number of studies performed concerning pathology in relation to the type of coping style adopted, there are some indications that the two coping styles differ in susceptibility to develop cardiovascular pathology, ulcer formation, stereotypies, and infectious disease.

## Cardiovascular Pathology

Various studies emphasize the differences between the two coping styles in autonomic balance. Because of the role of the two branches of the autonomic nervous system in cardiovascular control, one may expect a differential vulnerability for various types of cardiovascular pathology as well. Indeed, a number of experiments found evidence that the proactive coping animal is more vulnerable to develop hypertension, atherosclerosis, and tachyarrhythmia due to the high sympathetic reactivity (Fokkema, Koolhaas, & Gugten, 1995; Fokkema, Smit, Van der



Gugten, & Koolhaas, 1988; Manuck, Kaplan, & Clarkson, 1983; Sgoifo, De Boer, Haller, & Koolhaas, 1996; Sgoifo et al., 1997). However, it seems that these types of cardiovascular pathology only develop under conditions of threat to control rather than loss of control (Koolhaas & Bohus, 1991). The reactive coping style is characterized by a higher parasympathetic reactivity as can be observed by a strong bradycardia response in reaction to a sudden unexpected stressor. Although there have been no systematic studies of the cardiovascular consequences of this response, one may suggest that these types of animals are more vulnerable to sudden cardiac death.

### ***Gastric Ulceration***

The classical studies of Weiss, (1972) showed that the development of ulcers was high when the number of active coping attempts was high in the absence of informational feedback or with negative informational feedback present. In the experimental animal that could actively control the aversive shock by either pressing a lever during the warning signal or during the shock itself, the total length of stomach wall erosions was much smaller than in the yoked partner, which received exactly the same amount of shocks, but could not control them. Moreover, in the absence of informational feedback, a positive correlation was observed between the number of active coping attempts and the amount of gastric ulceration. In line with these results is an observation in the Roman high avoidance (RHA) and Roman low avoidance (RLA) rats, which can be considered to represent the proactive and reactive coping styles, respectively. It was shown that RHA rats, after stress of food deprivation for 5 days, had more stomach lesions than RLA rats (Driscoll, Martin, Kugler, & Baettig, 1983). A negative correlation between attack latency in the intruder test and gastric ulceration induced by restraint-in-water stress (Murison & Skjerve, 1992) also suggests that animals that prefer a proactive coping style are more vulnerable for the formation of ulcers during uncontrollable stress. In rat colonies, dominant animals that are usually representatives of the proactive coping style are reported to develop stomach wall erosions when they have lost their leading position (social outcast) after frequent attacks by other colony members. These studies suggest that the proactive individual is most vulnerable to stomach ulcers under conditions of loss of control. This observation is supported by studies in cattle (Wiepkema & Adrichem, 1987; Wiepkema & Schuiten, 1992).

### ***Immunologic Defense***

Contemporary psychoneuroimmunology emphasizes the role of the HPA axis and the sympathetic branch of the autonomic nervous system in the communication between the brain and the immune system (Felten et al., 1987). In view of the differential reactivity of these two systems in the two coping styles, one may expect

to see differences in the immune system as well. Indeed, several studies in rats and mice demonstrate that individual differentiation in coping is an important factor in stress and immunity. In particular in the social stress models, the individual level of social activity seems to be an important explanatory variable in some studies (Bohus & Koolhaas, 1990; Raab et al., 1986). Although these studies do not specifically address the issue of coping styles, it is tempting to consider the possibility that these socially active animals represent the proactive coping style. Sandi, Castanon, Vitiello, Neveu, and Mormede (1991) specifically addressed the question of the significance of individual differentiation in emotional responsiveness to the differentiation in immunology. They used the RHA and RLA rats that have been genetically selected on the basis of their active avoidance behavior (Driscoll, Demek, D'Angio, Claustre, & Scatton, 1990). These selection lines have been shown to differ in a number of behavioral and neuroendocrine stress responses in a similar way as the proactive and reactive coping styles as mentioned above. It was shown that the Natural Killer (NK) cell activity and the proliferation response of splenocytes to mitogenic stimulation was lowest in the RLA males, a difference that was even more pronounced after the stress of active shock avoidance learning. In a study of pigs, Hessing (1994) demonstrated that aggressive, resistant pigs had a higher *in vivo* and *in vitro* cell-mediated immune response to specific and nonspecific antigens than nonaggressive, nonresistant pigs. After stress, the aggressive, resistant pigs showed the strongest immunosuppression. This difference in immunologic reactivity in relation to coping style may explain the differential disease susceptibility in relation to social rank in group-housed pigs after a challenge with Aujeszky virus. These observations in pigs are consistent with similar data obtained in colony-housed male rats (Bohus & Koolhaas, 1990). Finally, it was demonstrated that proactive coping male rats are more vulnerable for the experimental induction of the autoimmune disease experimental allergic encephalomyelitis (EAE), which is considered to be an animal model for multiple sclerosis in humans. This high vulnerability seems to be due to the high sympathetic reactivity in the proactive coping males (Kavelaars, Heijnen, Tennekkes, Bruggink, & Koolhaas, 1999).

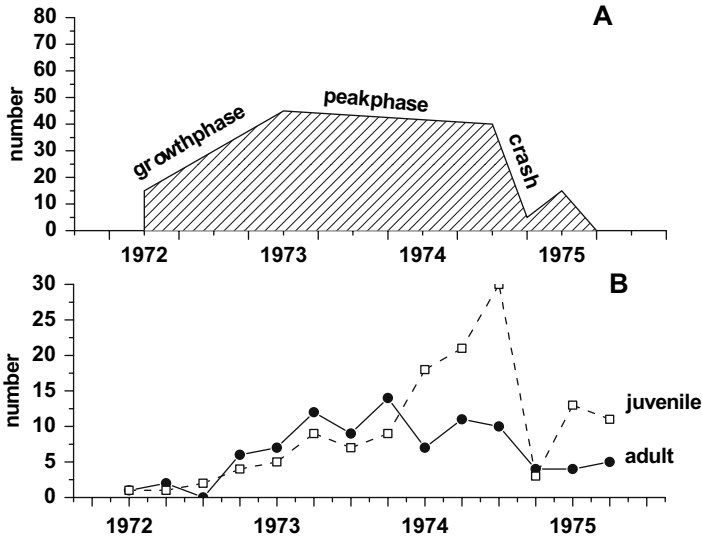
## Evolutionary Significance

Most of the data mentioned so far have been obtained using males under rather limited experimental conditions in the laboratory. To allow conclusions about the adaptive significance of coping strategies, one needs data from more complex natural populations as well. There are several examples in mammals, birds, and fish showing that phenotypic variation is somehow maintained within a single natural population. These field studies support the general view as outlined above on the adaptive significance of individual variation in behavior and physiology of animals. On the basis of extensive ecology studies in a sunfish species (*Lepomis gibbosus*), Coleman and Wilson (1998) found evidence that two morphologically different phenotypes occupy different habitats while both seem to have an advantage over

morphologically intermediate individuals. Subsequently, they considered the possibility that the same might be true for the individual differentiation in behavior, in particular for the differentiation in shy and bold animals. The way in which the distinction between shy and bold is described in a number of species, including monkeys, octopus, and fish, suggests that the shy individual might be similar to the reactive coping male, and the bold individual might be similar to the proactive copier. This leads to the question whether there is any evidence from rodent field studies that the proactive and reactive coping strategy have a differential adaptive significance. In feral mouse populations, there is some evidence that different behavioral phenotypes may have a differential fitness depending on the environmental conditions. In nature, mouse populations are known to go through phases of growth and decline. Such population cycles may cover a period from 4 to 7 years and can be so extreme that the population suddenly collapses at the end of a cycle and becomes extinct. Chitty (1967) hypothesized that the cyclic nature of rodent populations might be due to a disruptive selection for aggressive behavior in the course of the population cycle. Evidence that this might be the case was obtained in a study by Van Oortmerssen and Busser (1989) in seminatural populations of house mice consisting of both males and females. Phenotypic characterization of the laboratory-bred male offspring (F1) of fathers caught from these colonies revealed a bimodal distribution of attack latencies as measured in a standardized resident intruder paradigm. Subsequent selective breeding for high and low attack latencies resulted within five generations in a stable short attack latency (SAL) selection line. After a number of failures due to infertility of the offspring, we managed to obtain a long attack latency (LAL) selection line as well. Cross-fostering and back-cross experiments show that the phenotypic differentiation in aggressive behavior as observed in the colonies has a strong genetic basis.

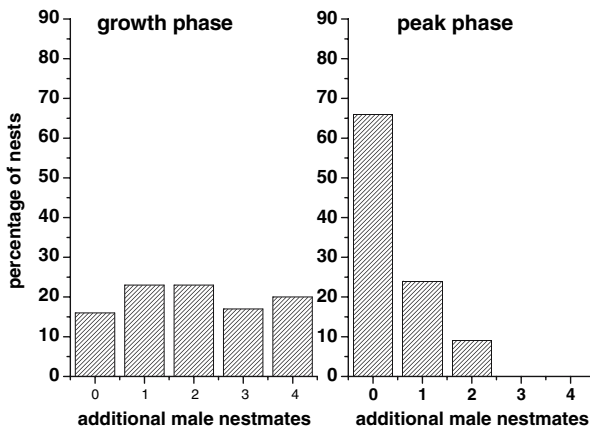
An analysis of the mortality reveals a strong increase in females, juveniles, and preweanling juveniles just before the crash of the population (Fig. 2.1). The idea that this increase in mortality is due to enhanced levels of aggression in the males is supported by an index of territoriality. Figure 2.2 shows the number of males present in the nests. In the growth phase of the population, on average four males were found together in each nest. Toward the crash, however, males were generally found alone, indicating a reduced tolerance for additional males in the nest. During the whole population cycle, animals are migrating from the population. It seems that the nonaggressive phenotype is more successful in establishing a new colony than the highly aggressive phenotype. This leads to the more general view that the two phenotypes observed in seminatural populations of house mice might have a differential fitness depending on the phase of the population cycle.

Recent studies in the great tit (*Parus major*), a small song bird, show a similar differentiation of phenotypes like in our rodent studies. Bold animals are relatively aggressive, superficial explorers and more prone to develop behavioral routines than shy birds. In a field study, Verbeek, Drent, and Wiepkema, (1994) observed a bimodal distribution of aggressive behavior of individual birds. Subsequent experiments showed that this differentiation has a genetic basis and can be considered behaviorally as a differentiation in proactive and reactive coping strategy.



**Fig. 2.1** (A) Change in population density of a feral population of house mice. (B) Mortality of adult and juvenile house mice during the various phase of the population cycle.

Observations in natural bird populations support the idea that the individual variation in coping strategy buffers the species against the negative effects of environmental variation such as food availability (Dingemanse, Both, Van Noordwijk, Rutten, & Drent, 2003). In this sense, the concept of coping strategies addresses a fundamental issue in evolutionary biology.



**Fig. 2.2** Number of males found together in one nest during the growth phase and at the end of the peak phase of a colony of wild house mice.

## Conclusion

Individual differentiation in behavior and physiology is a well-known phenomenon in many animal species. Unfortunately, there are relatively few studies using a more systematic approach to characterize individual response patterns across various environmental conditions. However, the scarce literature suggests that the dimension of proactive and reactive coping strategies can be distinguished in a wide variety of animal species (Koolhaas et al., 1999). Authors may use different terms to characterize phenotypes, such as shyness and boldness or proactive and reactive, but they all seem to share the same basic characteristics. Detailed analysis of coping strategies in rats and mice indicates that the most fundamental difference between proactive and reactive coping is the degree to which behavior is guided by feedback and feed-forward control. This results in a differential degree of behavioral flexibility. This degree of flexibility may have its origin in a differential survival value in nature. The challenge for the future is to integrate ethologic, stress physiologic, and ecologic approaches in the study of coping strategies.

From a biomedical point of view, the concept of coping strategies implies that different animals have a differential capacity to adapt to the same environmental conditions. Negative health consequences might arise if an animal cannot cope with the stressor or needs very demanding coping efforts. In view of the differential neuroendocrine reactivity and neurobiological makeup, one may expect different types of stress pathology to develop under conditions in which a particular coping strategy fails. Although there are only a limited number of studies performed concerning pathology in relation to the type of coping strategy adopted, there are some indications that the two coping strategies differ in susceptibility to develop cardiovascular pathology, ulcer formation, stereotypes, and infectious disease (Koolhaas et al., 1999).

If we accept the idea that nature somehow favors the existence of different phenotypes within one species, one may wonder how this relates to animals bred by humans in laboratory or animal husbandry conditions. Both in wild house mice and in a small bird, the great tit (*Parus major*), latency measures seem to have a bimodal distribution (Verbeek et al., 1994). Many studies use heavily domesticated animals that are usually selected for specific traits as well. In general, individual behavioral scores are normally distributed in these animals. Moreover, it is hard to tell how a certain inbred or domesticated strain relates to the original and presumably functional distribution of its wild ancestors. Nevertheless, it is intriguing that the extremes of this normal distribution often still fulfill the criteria for proactive and reactive coping strategies, both behaviorally and physiologically (De Boer, Van Der Vegt, & Koolhaas, 2003). Although the discussion on the shape of the distribution curve is important from an evolutionary point of view, it does not seem to matter much when the individual vulnerability to stress-related diseases is concerned. After all, it has been repeatedly shown that the extremes in a population, irrespective of the detailed distribution curve, may differ not only quantitatively but also qualitatively in their behavioral and physiologic response pattern to stress.

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